REMARKS

Applicants wish to thank the Examiner for the personal interview conducted on August 3, 2006, where no agreement was reached with respect to the claims. The interview was conducted in person and attended by Examiners Jill Warden and Dwayne K. Handy, and Applicants' representative Phil McGarrigle and Lisa T Kajisa. During the interview, applicants provided working examples of the chip device/holder as well as a description of the invention and a general discussion of the rejections applied under 35 U.S.C. §112. Both the Examiners and Applicants provided their respective interpretations of the supporting material for showing "whether or not there is sufficient support for the claimed feature of a chip having active sits on the chip surface that faces the cavity of the holder". As discussed and agreed upon, the Applicants filed an additional IDS which includes reference to an Interference Decision in a co-pending application on August 21, 2006. Applicants would like to state that the interview was found to be very helpful in advancing the prosecution of the present application.

Upon entry of this response, claims 141-167 are pending in the application and rejected under 35 USC §112.

Rejections under 35 – 35 U.S.C. §112

Claims 141-167 are rejected under 35 U.S.C. §112 as the description allegedly lacks support for showing "probes on the substrate facing the inside of the cavity of the holder". Applicants respectfully disagree with the Examiner for the reasons set out below.

Applicants respectfully assert that the above claim language is supported in the description of the first filed application and in the subsequent continuation and CIP applications and patents (i.e. 08/255,682, 08/528,173, 08/485,452 and 6,733,977) including the present application (10/789,678). For example, Applicants respectfully direct the Examiner's attention to claims 1, 14, and 35 of original parent application 08/255,682 filed June 8, 1994 as stated below. Sections below are underlined for emphasis.

> Claim #1. A method of making probe chips comprising the steps of: forming a plurality of probe arrays on a substrate; separating said substrate into a plurality of chips, each of said chips comprising at least one probe array thereon; and mating at least one of said chips to a package, said package comprising a reaction chamber, said reaction chamber comprising inlets for flowing fluid therein, said at least one probe array in fluid communication with said reaction chamber.
> Claim #14. The method as recited in claim 13 further comprising the steps of flowing labeled oligonucleotide target molecules through said reaction chamber and identifying where said target molecules have bound to said substrate.
> Claim #35. A method of evaluating probe chips comprising the steps of: forming a plurality of probe arrays on a substrate; separating said substrate into a plurality of chips, each of said chips comprising at least one probe array thereon; mating at least one of said chips to a package, said package comprising a reaction chamber, said reaction chamber in fluid communication with an inlet and outlet, said at least one probe array in fluid communication with said reaction chamber; and flowing labeled target molecules into said reaction chamber, said labeled target molecules reacting with said at least one probe array.

For another example, Applicants respectfully direct the Examiners to claim 1 in application 08/485,452, filed on 06/07/1994 which is a CIP of application 08/255,682.

> Claim #1. An apparatus for packaging a substrate, said apparatus comprising: a substrate having a first surface and a second surface, said first surface comprising a probe array and said second surface being an outer periphery of said first surface; a body having a mounting surface, an upper surface, and a cavity bounded by said mounting surface and said upper surface, said second surface being attached to said cavity and said first surface being within said cavity; and a cover attached to said mounting surface for defining an upper boundary to said cavity; wherein said cavity comprises a diffuser and a concentrator, said diffuser and said concentrator permitting laminar fluid flow through said cavity.

For the Examiners further consideration, Applicants set forth below examples claims from U.S. Patent number 6,733,977, which is also in the present chain of continuations from application number 08/485,452.

> Claim #1. An apparatus for hybridization of probe arrays, comprising: a substrate comprising a first surface and a second surface, said first surface comprising said probe array of biological polymers disposed thereon, said probe array comprising greater than 100 different probes at known locations on said first surface; and a housing comprising a mounting surface and a fluid cavity; said fluid cavity comprising an inlet port constructed to permit fluid flow into said cavity through said inlet port, wherein said first surface of said substrate is sealably mounted with respect to said mounting surface thereby sealably covering said cavity and whereby said probe array is located inside said cavity.
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> Claim #18. A method of hybridizing probe arrays comprising the acts of: providing a substrate comprising a first surface and a second surface, said first surface comprising said probe array of biological polymers disposed thereon, said probe array comprising greater than 100 different probes at known locations on said first surface; sealably mounting said substrate to a housing comprising a mounting surface and a fluid cavity; said fluid cavity comprising an inlet port constructed to permit fluid flow into said cavity through said inlet port, wherein said sealably mounting act provides said probe array located inside said cavity; and introducing said fluid inside said cavity to hybridize said probe array of biological polymers.

Applicants respectfully assert that the language is also supported in the description of the present application (10/789,678). For example, Applicants respectfully direct the Examiner to the following sections:

See section [0009] Page 1, 2nd column, Lines 35-43.

> "Typically, each chip contains at least one probe array. A chip is then mated to a package having a reaction chamber with fluid inlets. When mated, the probe array is in fluid communication with the reaction chamber.
> In a specific embodiment, the present invention provides an apparatus for packaging a substrate. The present apparatus includes a substrate having a first surface and a second surface. The first surface includes a probe array and the second surface is an outer periphery of the first surface. The present apparatus also includes a body having a mounting surface, an upper surface, and a cavity

bounded by the mounting surface and the upper surface. The second surface is attached to the cavity and the first surface is within the cavity."

See section [0101] Page 6 , 1st column, lines 48-60.

The chip packaging device provides an even distribution of fluid (or fluid flow) through the cavity over a top surface (or inner or active surface) of the chip. For example, a selected fluid enters channel 3207, flows through channel 3307, changes direction and flows through channel 3411, and evenly distributes into the cavity 3405 over the top surface of the chip. As previously noted, the cavity is defined by the flat bottom portion and cavity edges. A selected fluid exits the cavity by way of channel 3413, channel 3305, and channel 3205. The fluid flow over the top surface of the chip is preferably laminar, but may also be turbulent, a combination thereof or the like.

See section [0133] Page 9, 1st column, lines 13-16.

"Upon completion, the chip package will have a variety of uses. For example, the chip package will be useful in sequencing genetic material by hybridization. In sequencing by hybridization, the chip package is mounted on a hybridization station where it is connected to a fluid delivery system. Such system is connected to the package by inserting needles into the ports and puncturing the septums therein. In this manner, various fluids are introduced into the cavity for contacting the probes during the hybridization process."

See section [0080] Page 4, 2nd column, lines 7-14.

"Cavity 310 may include inlets 350 and 360. Selected fluids are introduced into and out of the cavity via the inlets. In some embodiments, the inlets are located at opposite ends of the cavity. This configuration improves fluid circulation and regulation of bubble formation in the cavity. The bubbles agitate the fluid, increasing the hybridization rate between the targets and complementary probe sequences. In one embodiment, the inlets are located at the top and bottom end of the cavity when the package is oriented vertically such as at the opposite corners of the cavity. Locating the inlet at the highest and lowest positions in the cavity facilitates the removal of bubbles from the cavity."

See section [0167] Page 11, lines 5-11.

"Next, the vortexer is activated to vibrate the chip package, similar to a paint mixer. In some embodiments, the vortexer may vibrate the package at about 3000 cycles per minutes. The motion mixes the targets in the fluid, shortening the

incubation period. In some embodiments, the vortexer rotates the chip package until hybridization is completed."

See section [0162] Page 11, lines 5-7.

"In operation, a fluid is placed into container 2810. The fluid, for example, may contain targets that are to be hybridized with probes on the chip."

See section [0155]

"FIGS. 27a-27b illustrate an alternative embodiment of the package. FIG. 27a illustrates a top view and FIG. 27b shows a cross sectional view. As shown, package 2700 includes a cavity 2710 on a surface 2705. A chip 2790 having an array of probes 2795 on surface 2791 is mated to the bottom of cavity 2710 with an adhesive 2741. The adhesive, for example, may be silicone, adhesive tape, or other adhesive. Alternatively, clips or other mounting techniques may be employed. Optionally, the bottom of the cavity may include a depression in which a chip is seated."

The passages above show that a probe array is constructed on a substrate and that the array is attached to a reaction chamber with the array facing inside of the chamber. It is further shown that targets are introduced into the chamber and hybridized to the array emphasizing that the probes are located inside the chamber. For the above reasons, withdrawal of the rejection of claims 141-167 is respectfully requested.

Conclusion

No new matter has been added with this amendment. Consequently, Applicants have responded to the outstanding rejections. They respectfully request that the Examiner reconsider and withdraw the present rejections and pass the present application to issuance.

For these reasons, Applicants believe all pending claims are now in condition for allowance. If the Examiner has any questions pertaining to this application or feels that a telephone conference would expedite prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000. Applicants are also providing a terminal disclaimer with this response.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

Respectfully submitted,

Date: 10/17/06

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